PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WJW6109805	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 02/05842	International filing date *(day/month/year)* 20.12.2002	Priority date *(day/month/year)* 20.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/404		
Applicant CANCER RESEARCH TECHNOLOGY LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.06.2004	29.10.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Scruton-Evans, I Telephone No. +49 89 2399-8272

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 02/05842

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-114	as originally filed

Claims, Numbers

2-89	as originally filed
1	as amended (together with any statement) under Art. 19 PCT

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 83-89

   because:

   ☒ the said international application, or the said claims Nos. 83-89 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-89
	No:	Claims	
Inventive step (IS)	Yes:	Claims	65-77
	No:	Claims	1-64,78-89
Industrial applicability (IA)	Yes:	Claims	1-82
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 83-89 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents cited in the search report are referred to in this communication;

D1: Bioorganic & Medicinal Chemistry Letters, Oxford, Gb (03-2000), 10(5), 513-515
D2: US-A-5391570
D3: WO-A-03004479
D4: EP-A-0469984

Document D3 was published after the filing date of the present application, and will thus not be taken into consideration for this opinion.
The correction of the beta bond in the Article 19 PCT claim 1 is accepted, and corresponds to that subject matter that was searched.
With regard to the requirement for novelty (Article 33(2) of the PCT); the compounds of the present application differ from those of D1 and D2 in the indol-2-yl group, and from D4 in the indole instead of indoline and the cyclohexa-4-one group. Article 33(2) thus appears to have been satisfied.

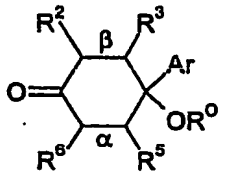
With regard to the requirement for inventive step (Article 33(3) of the PCT), the compounds of the present application that have actually been shown to provide a solution to the problem of providing novel compounds with thioredoxin inhibitory activity and antiproliferative/anticancer activity can be considered to represent a non-obvious solution to the problem of the provision of novel compounds with this activity, and thus inventive according tot Article 33(3) of the PCT: However, the extrapolation over the specific examples to the scope of the claim wherein such broad definitions and

undefined groups are used (it is assumed that the group Ar can be substituted (see claim 34)) is not considered to have been justified, and thus Article 33(2) of the PCT can only be considered to have been satisfied at this stage for the specific compounds of claims 65-77.
For the assessment of the present claims 83-89 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claims 65-77 make reference to the description, and claim 34 does not define any of the substituents other than as a substituent (Article 6 and Rule 6.2 PCT)

CLAIMS

1. A compound having the following formula:



(1)

wherein:

Ar is a 1-(sulfonyl)-1H-indol-2-yl group;

the group $-OR^O$ is independently:

(a) -OH;

(b) an ether group; or:

(c) an acyloxy group;

the bond marked α is independently:

(a) a single bond; or:

(b) a double bond;

the bond marked β is independently:

(a) a single bond; or:

(b) a double bond;

each of R^2, R^3, R^5, and R^6, is independently a ring substituent and is:

(a) H;

(b) a monovalent monodentate substituent; or:

(c) a ring substituent which, together with an adjacent ring substituent, and together with the ring atoms to which these ring substituents are attached, form a fused ring;

and pharmaceutically acceptable salts, esters, amides, solvates, hydrates, and protected forms thereof.

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